UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/927,315	08/10/2001	Charles S. Zuker	02307E-120110US	4699

20350 7590 08/26/2003

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER
BRANNOCK, MICHAEL T

ART UNIT	PAPER NUMBER
1646	13

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/927,315	ZUKER ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *09 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-74* is/are pending in the application.

4a) Of the above claim(s) *1-30,34-48 and 52-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *31-33,49-51 and 55-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *10 August 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application: Claims and Amendments

Applicant is notified that the amendments put forth in Paper 12, 5/9/03, have been entered in full.

Claims 1-74 are pending. Claims 1-30, 34-48, 52,-54 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12.

Applicant's election with traverse of Group VII, as the claims relate to a heterodimer of SEQ ID NO: 9 and 15, is acknowledged. The traversal is on the grounds that a search of Groups I-VII would not be a serious burden on the examiner. This is not found persuasive for the following reasons:

Under MPEP § 803, there are two criteria for a proper requirement for restriction between patentably distinct inventions:

(A) The inventions must be independent (see MPEP § 8702.01, 806.04, 808.01) or distinct as claimed (see MPEP § 806.05- §806.05(I)): and

(B) There must be a serious burden on the examiner if restriction is required (see MPEP § 803.02, § 806.04(a)- 806.04(I), § 808.01(a), and § 808.02).

Consistent with current patent practice, a serious search burden may be established by (A) separate classification thereof: (B) a separate status in the art when they are classifiable together: (C) a different field of search. These criteria were met in the above restriction. Further, a search is directed not only to art which would be anticipatory, but also to art that would render the invention obvious. In the instant case, although a search of the methods of

Group VII would overlap a search of the other groups, no two searches would be coextensive. Thus, Groups I-VII require divergent searches, and to search all of the inventions would be burdensome. In particular, Applicant asserts that a search of the method of Group VII would necessarily identify all of the art relevant for the peptides of Group III. This argument has been fully considered but not deemed persuasive. Although the two searches would overlap, they would not be coextensive as evidenced, for example, their separate classification in the art. Therefore, the restriction is maintained and made final.

Additionally, Applicant is reminded that the claims will be examined only to the extent that the claims are directed to the elected SEQ ID NO: 9 and 15. Applicant asserts that if the examiner finds such subject matter free of the prior art, then the other non-elected species will examined. This assertion is not correct. The species identified by the examiner are independent and distinct inventions, as indicated in the previous office action. Only upon the allowance of a generic or linking claim, would the other species be searched, see MPEP 809.

Drawings

The drawings are objected to as set forth in the attached Notice of Draftsperson's Patent Drawing Review (PTO-948). A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119 and 120 as follows: The Bibliographic Data Sheet

indicates that priority is claimed to 60/302,898, yet the first paragraphs of the specification indicate that the application is "related" to several other applications. This is improper, see MPEP § 20.11.

> If applicant desires priority under 35 U.S.C. 119e or 120 based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months

from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink(s) and/or other form of browser-executable code, e.g. page 16. See MPEP § 608.01.

Claim Objections

Claims 31-33 are objected to as being dependent from a nonelected base claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 31-33, 49-51, 55-74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the following reasons.

(A)The claims require "modulators" of taste transduction, however the specification does not set forth what a modulator is. At page 13 the specification sets forth that compounds can be activators, inhibitors, or modulators of taste transduction, thus it appears that the specification contemplates compounds that have properties other than that of an activator or inhibitor; what these properties are is not stated. Thus, the artisan would not know whether he or she was practicing the claimed invention.

(B)Claims 31-32, 49-51, 55-74 require "moderately stringent conditions" The term "moderately stringent conditions" is confusing because it is a relative term and encompasses conditions of varying degrees of stringency - such conditions determining the bounds of the claim. However, the art does not provide an unambiguous definition of the term "moderately stringent conditions" and neither is such a definition given for the term in the specification which puts forth the metes and bounds of the claim Applicant is seeking protection for. At page 20, it appears that the specification specifically defines the term "highly stringent conditions", i.e. conditions wherein a probe will hybridize to its target sequence but to no other sequences. However, at page 21, the specification provides only an example of "moderately stringent

conditions" yet this example cannot define the bounds of the term, and therefore the bounds of the claims is undeterminable. It is suggested that the claim recite the actual conditions that applicant considers to be moderately stringent, i.e., salt concentration and temperature conditions of incubations and washes.

(C) As now amended, Claim 33 lacks antecedent basis for the term "the T1R2 polypeptide"; additionally Claims 31 and 32 lack antecedent basis for the term "heterologous polypeptide".

(D) Claims 55-74 require a "functional effect", although the specification recites several examples of "functional effects" the skilled artisan could not be sure whether or not he or she was practicing the claimed invention because of the presence of such an ambiguous term.

(E) Claim 64 requires "*the* extracellular domain". The art does not appear to recognize that a GPCR has what could be called "the extracellular domain" as would a single pass protein such as a receptor tyrosine kinase. Rather, it is well established that a GPCR has several extracellular domains because it snakes though the membrane seven times. Thus, amendment to the claims to require "*an* extracellular domain" instead of "the extracellular domain" would obviate this part of the rejection.

(F) Claim 65, and dependent claims, require that the protein be expressed in a cell or cell membrane, however it is not clear if the claimed method must be practiced while the protein is in a cell or cell membrane, or whether it simply means that the protein be expressed in a cell or cell membrane and then purified, as opposed to, e.g., a cell free translation.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31-33, 49-51, 55-74 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of identifying activators and inhibitors of sweet taste signal transduction, comprising a taste cell receptor composed of a heterodimer of SEQ ID NO: 9 and 15, wherein the receptor is present on the surface of a cell, and wherein the receptor is coupled to a Gα15 protein, does not reasonably provide enablement for methods employing artificially constructed variants of SEQ ID NO: 9 and 15, and nor for methods wherein the receptor is attached to a solid support, and nor for methods of identifying *modulators* of taste signal transduction. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

(A) The claims encompass the use polypeptide variants of the polypeptides of SEQ ID NO: 9 and 15 (substitutions, deletions or insertions in a protein corresponding to SEQ ID NO: 9 or 15) i.e. protein variants encoded polynucleotides that need only hybridize to a polynucleotide encoding SEQ ID NO: 9 and 15. Although the specification indicates that such variants are encompassed by the invention (e.g. page 5), no specific teaching is provided to indicate which amino acid substitutions, deletions or insertions to make. The specification has not provided sufficient guidance as to how to make and use the encoded polypeptides which are not 100% identical to the polypeptide of SEQ ID NO: 9 or 15, but which still retain a desired property of

the polypeptide of SEQ ID NO: 9 or 15. Furthermore, the specification has not provided guidance as to what properties of the allelic variants or sequence variants of the protein corresponding to SEQ ID NO: 9 or 15 might be desired nor any guidance as to which amino acid substitutions, deletions or insertions to make to achieve any desired property. Applicant has not defined a difference in structure or difference in function between the proteins corresponding to SEQ ID NO: 9 and 15 and variants of said proteins. If a variant of a protein corresponding to SEQ ID NO: 9 or 15 is to have a structure and function similar to a protein corresponding to SEQ ID NO: 9 or 15, then the specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make that will preserve the structure and function of a protein corresponding to SEQ ID NO: 9 or 15. Conversely, if a protein variant of SEQ ID NO: 9 or 15 need not have a disclosed property, the specification has failed to teach how to use such a variant.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see Bowie et al., 1990, Science 247:1306-1310, especially p.1306, column 2, paragraph 2). However, Applicant has provided little or no

guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions.

Although the specification provides the suggestion that such variants can be obtained, this is not adequate guidance as to the nature of active variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity.

The claims are, in essence, single means claims, because the claims encompass any composition having the recited activities whereas the instant specification only discloses those naturally occurring compositions known to the inventor, i.e. SEQ ID NO: 9 and 15. In *In re Hyatt*, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983), a single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification at most disclosed only those means known to the inventors. When claims depend on a recited property, a fact situation comparable to *Hyatt* is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. See also *Fiers v. Sugano*, 984 F.2d 164, 25 USPQ2d 1601 (Fed. Cir. 1993), and MPEP § 2164.08(a).

With regard to enablement for artificially constructed variants of the polypeptides of SEQ ID NO: 9 and 15, the instant fact pattern is actually one step removed and deficient from that of *Hyatt*. The instant specification does not disclose any working examples of artificially constructed variants of the polypeptides encoded by SEQ ID NO: 9 and 15.

(B) The claims encompass methods of identifying sweet taste modulators wherein the receptor is not present in the membrane of the cell, e.g. claim 62 requires that the receptor be attached to a solid support. Thus, the receptor would somehow need to make an appropriate response to a ligand when the receptor was attached to a solid support. No specific guidance is provided as to what methods can be used to accomplish this. The art recognizes the difficulty in establishing functional responses of taste receptor G-protein coupled receptors. It does not appear to be routine in the art to produce functional responses from such receptors in anything other than the membrane of the cell, see page 382, col 1, middle paragraph of Lindemann, B. Nature Medicine 5(4)381-382, for example. In this regard the claims are also single means claims, because the claims encompass any method having the recited activities whereas the instant specification only discloses the single method known to the inventor.

(C) The specification puts forth that the sweet receptor can be coupled to a G-protein or a promiscuous Gα15 G-protein (see page12, line 23), however the only particular G-protein that is taught to work in the claimed invention is Gα15. The claims encompass, and the specification contemplates, using other G-proteins. The claims encompass the use of the endogenous G-protein(s) and the skilled artisan appreciates that such a use would be desirable, yet the specification has not provided any, and nor is such known in the prior art. Essentially, therefore, the specification has merely invited the skilled artisan to embark on an extensive research plan to

try to find other G-proteins that would work in the invention. Such a call for extensive trial and error experimentation places an undue burden on the skilled artisan trying to practice the invention commensurate with the scope of what is being claimed. Additionally, in this regard the claims are also single means claims, because the claims encompass any method having the recited activities whereas the instant specification only discloses the single method known to the inventor.

(D) As set forth above in item (A) of the rejection under 35 U.S.C. 112, second paragraph, the specification appears to make a distinction between the genus of compounds considered to be activators and inhibitors of sweet taste signal transduction and the genus of compounds that would be considered "modulators" of sweet taste transduction. It is unclear what this distinction is, if any. A reasonable interpretation is that "modulators" include the ability to transform the perception of taste from one quality to another, e.g. to "customize taste" (page 10, L25). For example, a modulator might, when present, make the taste of saccharin more like the taste of sucrose. Without trying to read limitations into the claims that are not there, one can only guess at what is intended to be encompassed by the intended distinction between "modulators" and "activated or inhibitors". Regardless, the specification has provided sufficient guidance only for assays that identify activators and inhibitors of sweet taste signal transduction as defined in the specification at page 13, L26 – page 14, L1.

Due to the large quantity of experimentation necessary to generate the infinite number of variants recited in the claims and screen same for activity, the lack of direction/guidance presented in the specification regarding G-proteins, solid supports and assays wherein the protein is not in a membrane, and modulators, the absence of working examples directed to same, the

complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function and also the functionality of taste receptors in assay systems, and the breadth of the claims which fail to recite significant structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 31-33, 49, 50, 55-57, 59, 65 and 71-73 are rejected under 35 U.S.C. 102(b) as being anticipated by Kinnamon, SC et al., Current Opinion in Neurobiology 6(506-513)1996. The claims do not require that the receptor be purified or recombinant and the specification indicates that the receptor is a human sweet receptor present in a human tongue. Thus, the claims read on any method that assays the functional effects of contacting the receptor with candidate compounds. Such methods have, of course, been practiced for centuries. Kinnamon et al. review the more modern methods involving in vivo, ex vivo, and in vitro methods wherein the

physical and chemical effects of tastants are assayed, see page 509 under the heading "Sweet stimuli" for example.

Conclusion

No claims are allowable.

Please note the new official fax number below:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (703) 306-5876. The examiner can normally be reached on Mondays through Thursdays from 8:00 a.m. to 5:30 p.m. The examiner can also normally be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

August 22, 2003

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600